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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09 608,713	06/30/2000	Hideo Ago	SHVL-007	2086

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EXAMINER	
LY, CHEYNE D	
ART UNIT	PAPER NUMBER

DATE MAILED 02/26/2003

19

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)	
09/608 713	AGO ET AL	
Examiner	Art Unit	
Cheyne D Ly	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on December 09, 2002
- 2a) ☐ This action is **FINAL** 2b) ☒ This action is non-final
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213

Disposition of Claims

- 4) ☒ Claim(s) 19-36 is/are pending in the application.
- 4a) Of the above claim(s) 19-29, 32 and 34-36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 30, 31 and 33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 19-36 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of
- 1 ☐ Certified copies of the priority documents have been received
- 2 ☐ Certified copies of the priority documents have been received in Application No. _____
- 3 ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a))
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application)
- a) ☐ The translation of the foreign language provisional application has been received
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 & 18
- 4) ☐ Interview Summary (PTO-413) Paper No(s) 15 & 16
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other

DETAILED ACTION

1. Applicants' arguments in Paper No. 17, filed December 09, 2002, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.
2. Claims 30, 31 and 33 are examined on the merits.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. This rejection is maintained with respect to Claims 30, 31 and 33 as recited in the previous office action Paper No. 14, mailed September 26, 2002.
5. It is acknowledged that applicants have disclosed information to enable one skilled in the art to make a crystal of the HCV polymerase using NS5B^{570-544-536 and 531} (Examples 1-3, Pages 20-27). Further, Applicants provide abstracts to publications to support the predictability of the art of crystallizing HCV polymerase. Therefore, Applicants argue that the disclosure and cited support enable the full scope of the claims 30, 31 and 33 regard to the limitations of the method for identifying a HCV polymerase inhibitor. Applicants' arguments, pointed enablement support for NS5B^{570-544-536 and 531} and cited publications have been fully considered and they have been found to be unpersuasive.

6. As cited in Paper No. 14, mailed September 26, 2002, it is well documented that protein crystallization is in essence a trial-and-error method, and the results are usually unpredictable (Drenth, J.). Further, as recently as November 1, 2002, Science published a *New Focus* article depicting the current state of the art for protein crystallization that supports the unpredictability of the art. In essence, protein crystallization is still a trial and error process because the current technology for producing protein for the crystallization process is unpredictable, which results in high failure rate for proteins that are being crystallized. Therefore, researchers continue to have trouble generating sufficient protein required for the crystallization process (Science, 2002). The citation of a few successful but isolated crystal structures of HIV polymerase does not help the instant applicant to overcome the overwhelming evidence provided by *New Focus* stating the unpredictability of the art of protein crystallization. For example, "[s]o far, these projects have targeted more than 18,000 proteins but solved the structures of only about 200" (Page 948, Column 3, lines 4-6). Therefore, it is further re-iterated that it is unreasonable to expect one skilled in the art to use the information disclosed for one specific crystal to make other of predictable quality that are different from the crystal disclosed in the specification without undue experimentation.

7. Claim 33 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

8. The introduction of lines 18 and 19 is considered to be new matter. It is acknowledged that Applicants disclose a method for the identification of inhibitors for the HCV polymerase (Example 7, pages 280-282). It is further acknowledged that Applicants disclose "[t]he difference of the HCV polymerase activities was observed...are particular effective as HCV polymerase inhibitors" (Page 280, lines 13-16). However, the specification of the instant application does not disclose, "wherein an activity determined in step(b) that is lower than the HCV polymerase activity determined in step(c)". The Examiner interprets the disclosure of "the difference of the HCV polymerase activities was observed" to indicate HCV that polymerase activities could be lower or higher but not just lower for a test compound to be identified as an inhibitor of HCV polymerase.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 33 recites the limitation "the test agent" in line 19. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(c), (f) or (g) prior art under 35 U.S.C. 103(a).
3. Claims 30, 31 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over US006183121B1 in view of In re Gulack, 703 F.2d 1381, 1385, 217 USPQ 401, 404 (Fed. Cir. 1983) taken with Bressanelli et al. (1999).
4. Kim et al. discloses a method that uses "atomic coordinates of all the amino acids of NS3 helicase according to FIG. 1, \pm , a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 \AA NG., to generate a three-dimensional structure of molecule comprising a NS3 helicase-like binding pocket. For the first time, the present invention permits the use of molecular design techniques to identify, select and design chemical entities, including inhibitory compounds, capable of binding to NS3 helicase-like binding pockets—in particular, the oligonucleotide binding pocket of NS3 helicase" (Column 14, lines 27-38). "Thus, any compound which fits into a pocket comprising the structural coordinates \pm , a root mean square of 1.5 \AA NG. or less from the backbone atoms of these amino acids is a potential inhibitor of the NS3 helicase" and data disclosed in Table 1 suggest the inhibitory nature of potential

inhibitors (Column 31, 36-45 and Table 1). Even though the method disclosed by Kim et al. does not specify that the three-dimensional structural coordinate is derived from a HCV polymerase, the specific limitations of three-dimensional structural coordinate is derived from a HCV polymerase in this instant case do not distinguish the invention from the prior art in term of patentability because they are descriptive nonfunctional subject matter.

5. In re Gulack defines nonfunctional descriptive material, as when descriptive material is not functionally related to the substrate, the descriptive material will not distinguish the invention from the prior art in term of patentability. Also, the MPEP indicates that descriptive material that cannot exhibit any functional interrelationship with the way in which computing processes are performed does not constitute a statutory process, machine, manufacture or composition (MPEP § 2106 (IV)(B)(b)). Specific to the instant case, the three-dimensional structural coordinates derived from a HCV polymerase of a method for identifying a HCV polymerase inhibitor are merely stored so as to be read or outputted by a computer without creating any functional interrelationship, either as part of the stored data or as part of the active steps of the method for identifying a HCV polymerase inhibitor, then such descriptive material alone does not impart functionality either to the data as so structured, or to the computer.
6. Bressanelli et al. discloses a crystal structure of the RNA-dependent RNA polymerase of hepatitis C virus where the catalytic domain of the HCV RdRp consists of the 531 amino-terminal residues of NS5B. As a key step to developing specific anti-HCV drugs that interfere with viral replication (Page 13034, lines 23-26).

7. Clearly, a skilled artisan would have been motivated to partake the concept emphasized by Kim et al. for a method that uses of molecular design techniques to identify, select and design chemical entities, including inhibitory compounds based on the 3-dimensional structure of a polymerase and apply such method to the crystal structure for RNA-dependent RNA polymerase of hepatitis C virus as disclosed by Bressanelli et al. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use the method taught by Kim et al. with the crystal structure coordinates of the RNA-dependent RNA polymerase of hepatitis C virus disclosed by Bressanelli et al. for identifying a HCV polymerase inhibitor.

CONCLUSION

8. NO CLAIM IS ALLOWED.
9. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CMI Fax Center number is either (703) 308-4242 or (703) 305-3014.
10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (703) 308-3880. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.
11. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

12. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

C. Dune Ly
2/13/03

Adrian W. Marschel
2/13/03